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## De pseudobromuriden van brocq, pautrier en fernet, een vorm van blastomycose

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## Summary.

In connection with a case of the "pseudo-bromurides" of BROcq, PAUTRIER, and FERNET observed by me, I have drawn attention to this rare disease, of which BROcq, after the first publication in 1909, published three other cases, and of which no other mention is made in the literature. The skin-eruptions in this disease have at first a very typical form, which is clearly seen in the photographs of mij patient. These efflorescences rapidly become larger, and change into serpiginous, peripherally progressive, vast ulcers with a granular base. Among the granulations there are openings, from which pus makes its appearance. The skin affections remind one in the first place of those which are sometimes seen to occur after the internal use of bromides. Hence the name. However in the cases of BROcq the use of bromides or iodides could be excluded. This is also the case with the patient observed by me. BROcq further thought most of an affection caused by staphylococci, or of a systemic mycosis. BROcq was able to raise various strains of staphylococci from the pus, but no fungi. No staphylococci could be raised from the blood. The histological aspect

of the affections at various stages showed no tuberculoid structure, as is seen in various cases of mycosis, but only symptoms of acute or sub-acute inflammation. The general condition of the patients is bad. Of the patients observed by BROCC three died. The issue of the fourth case is not known. In the case of my patient, who was in a very bad general condition, but who later recovered, it was also impossible to raise any fungi from the pus. The pus was likewise found to be free from staphylococci, when it was taken from new, closed efflorescences. The histological preparation from the eruptions showed symptoms of sub-acute or acute inflammation at all stages, with hyperplasia and downgrowth of the epidermis, and micro-abscesses. Tuberculoid structure, giant cells, or parasites could not be demonstrated in the preparations. I was however able to raise a yeast-like fungus from the blood.

On subcutaneous injection with killed culture-material from this fungus, the patient reacted with violent redness at the point of injection. A few days later an eruption broke out here, bearing a great resemblance to the spontaneously occurring efflorescences, and very soon differing from these in no respect whatever. In later tests the patient also invariably showed a violent reaction, and as a rule an eruption occurred of the same sort as the lesions which occurred spontaneously at the same period. A control person did not react to the same injections. The patient did not react to injections with killed culture-material from another fungus, a pathogenic *Monilia* strain. After her recovery the patient no longer reacted to the injections with the fungus raised from her own blood.

Complement fixing reactions with antigens prepared in various ways gave negative or not specific, slight positive reactions. It was impossible to apply agglutination tests, as I did not succeed in obtaining a good suspension of the fungus.

Subcutaneous inoculation with the fungus caused a large abscess to occur in a rabbit, in which it was possible to demonstrate fungus elements.

Yeast-like organisms were found in catheter urine. In the sputum mycelial threads and budding cells were observed. The



physical examination of the chest suggested the existence of pulmonary tuberculosis. Animal tests with the sputum had, however, a negative result. Tuberculosis bacilli were not found in the sputum. The x-ray photo showed that there was somewhat more shadow on the right side than on the left.

Dr. GOEDHART observed a patient at the Hague, who greatly resembled my case. Here, too, a bromo- or iododerma, or even a mycosis, was suspected. The first was shown by the past history to be out of the question. The test of the pus for fungi had a negative result. Only a number of staphylococcus strains were raised. The histological examination of the skin-lesions showed about the same aspect as in the case of my patient. This patient also had pulmonary affections but of a more serious nature. The symptoms suggested a pulmonary abscess. There were haemorrhagic sputa. A dense shadow was visible in the röntgen photo. In this case, also, mycelial threads and budding forms were found in the sputum. The presence of pulmonary affections with yeast-like fungi in the sputum suggested the possibility of a direct connection with the skin-eruptions. I did not succeed in isolating a fungus from the sputum of my patient which was certainly identical with that raised from the blood. This latter was however able to cause an affection in the case of a rabbit, after the animal had been given an intrapulmonary injection, which affection corresponded entirely with the one mentioned by CASTELLANI as the result of an intrapulmonary injection with fungi which cause bronchomoniliasis. A similar affection developed in the case of another rabbit in the mediastinum. This animal developed after some time multiple cutaneous abscesses. Fungi were found in the lesions of lungs and mediastinum, but not in the cutaneous abscesses. The sick rabbit showed an allergic reaction following an injection with killed culture material in one ear, but not after an injection with another fungus, a *Monilia* strain. A healthy rabbit did not react to injections with the same fungi. The histological preparation of the lesions in the case of the rabbit showed no tuberculoid structure, but exclusively symptoms of acute and sub-acute inflammation, as in the case of both patients.

As in several cases of blastomycosis the primary focus is present in the lungs, there is a great probability, in this case of mine and in that of Dr. GOEDHART, that here, also, an affection very closely related to the bronchomoniliasis of CASTELLANI was primarily present, after which the cutaneous eruptions broke out secondarily. The results of the tests on animals lend every support to this view. It does not follow from this that all cases of "pseudo-bromurides" are secondary to a mycosis of the respiration tract. The primary focus may also be situated elsewhere. The absence of demonstrable fungi suggests the possibility that the affection is to be regarded as the result of an allergic reaction of the skin on dead or weak fungus elements which have arrived there through the blood circulation, and which are in themselves only slightly virulent. A parallel may then be drawn between this affection and the tuberculides. A similar phenomenon is known with other mycoses (trichophytides, microsporides). The affections described might in that case be called „blastomycides". Just as in the case of the tuberculides the histological aspect of the lesions corresponds to a particular allergic condition of the skin, the same connection is possible here. By allergia any changed reactive capacity of the skin may be understood. The positive anergia, which as a rule is found with the miliary lupoides of BOECK, is thus also a form of allergia. This form, which manifests itself as a hypersensitive reaction, might be called "hyperergia", to distinguish it from the former. With tuberculides a predominance of acute inflammation symptoms is often accompanied by a "hyperergic" skin-reaction. A logical connection between the two is, as has been shown by various investigators, probable. It may obviously be assumed that the same connection exists between the strong "hyperergic" skin-reaction in the case of my patient, and the exclusive presence of acute inflammation symptoms in the histological preparation from the lesions, so that the absence of tuberculoid structure and giant cells does not necessarily militate against the diagnosis blastomycosis.

The form of the fungus raised on various media is described in detail. The photographs appended speak for themselves. The



fungus was found not to form asci. It consists of budding forms and branched mycelial threads with septa. By means of some special methods of investigation, described in detail, it was possible to ascertain that the fungus forms arthrospores at the end and in the middle of the hyphae. Sugars are not fermented. Litmus whey becomes slowly acid. Milk is not clotted. Serum is not, gelatine only slowly liquefied. In liquid media no surface film is formed. The fungus is only slightly pathogenic for animals. On the strength of its qualities it forms a transition between the *Blastosporineae* and the *Arthrosporineae*, for which reason I transfer it to the genus *Parendomyces*, which OTA suggested, in 1924, to be used for such transition forms between the two sub-orders mentioned. I do not wish to identify this genus with the genus *Trichosporum*, as OTA did two years later. This name had till then been used for a "medical genus", the characters of which were based on the symptoms caused by the parasites in patients. (Other "medical genera" are, e.g., the genera *Achorion*, *Epidermophyton*, and others.) Although I prefer a botanical classification, it seems to me to be confusing to employ the same name *Trichosporum* for a newly-created "botanical genus" which has quite different characters. I therefore consider it preferable, to retain the genus *Parendomyces* for those fungi which, possessing yeast-like cells, mycelial threads, and arthrospores, form a transition between the *Blastosporineae* and the *Arthrosporineae*.

I have called the fungus *Parendomyces brocqii*, in honour of the memory of the great dermatologist, who, together with his co-operators, first described the disease.

Therapeutically iodides seem to me to be indicated in this disease, since both my patient and that of Dr. GOEDHART recovered, mine after copious administration of sodium iodide per os, Dr. GOEDHART's after the use of rather small doses of potassium iodide. These therapeutic successes proved that the effect of iodides is not produced only when a specific granulation tissue is present, as STEIN considers. A vaccine was employed in the

later disease-period of my patient. To what extent this promoted the process of recovery it is impossible to determine.

After recovery the patient showed atrophic, white scars, with small retractions, as NEUBER also describes in the case of blastomycosis observed by him.

All the known forms of mycosis were studied in detail, in order to determine whether the disease of BROcq, PAUTRIER, and FERNET might not be the same as one of these affections. It was found, however, that this disease could claim a place of its own. This affection might be called a "parendomycosis" or "parendomycide", from the name I have given to the fungus found. I am however convinced that any classification of the yeast-like microorganisms at the moment must still be considered provisional, so that it is better not as yet to name the diseases caused by these parasites after the names of the fungi now in use. I therefore propose to continue calling the disease "pseudo-bromurides of BROcq, PAUTRIER and FERNET, a form of blastomycosis".